

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 04 October 1996 (04.10.96)	
International application No. PCT/US96/02153	Applicant's or agent's file reference LKS94-04A2
International filing date (day/month/year) 12 February 1996 (12.02.96)	Priority date (day/month/year) 10 February 1995 (10.02.95)
Applicant BRISKIN, Michael, J. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

09 September 1996 (09.09.96)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Ting Zhao

Telephone No.: (41-22) 730.91.11

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference LKS94-04A2	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 96/ 02153	International filing date (day/month/year) 12/02/96	(Earliest) Priority Date (day/month/year) 10/02/95
Applicant LEUKOSITE, INC. et al.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☒ Certain claims were found unsearchable (see Box I).

2. ☐ Unity of invention is lacking (see Box II).

3. ☒ The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing

☒ filed with the international application.

☐ furnished by the applicant separately from the international application,

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the **title**, ☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:

Figure No. _____ ☐ as suggested by the applicant.

☐ None of the figures.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 96/02153

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 51-100
because they relate to subject matter not required to be searched by this Authority, namely:
REMARK: ALTHOUGH CLAIMS 51-100 ARE DIRECTED TO A METHOD OF TREATMENT OF THE HUMAN BODY THE SEARCH HAS BEEN CARRIED OUT AND BASED ON THE ALLEGED EFFECTS OF THE COMPOSITION.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/IS 96/02153

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C07K14/705 C12N15/62 C07K19/00 C07K16/28
G01N33/566

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO,A,94 13312 (THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY) 23 June 1994 see the whole document ---	1-100
A	JOURNAL OF IMMUNOLOGY, vol. 153, no. 1, 1 July 1994, BALTIMORE US, pages 517-527, XP002006075 D.J.ERLE ET AL.: "Expression and function of the MAdCAM-1 receptor, integrin alpha4beta7, on human leukocytes" see page 525, left-hand column --- -/--	1-100

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

19 June 1996

Date of mailing of the international search report

27.06.96

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+ 31-70) 340-3016

Authorized officer

Cupido, M

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 96/02153

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>NATURE, vol. 363, 3 June 1993, LONDON GB, pages 461-464, XP002006076 M.J.BRISKIN ET AL.: "MAdCAM-1 has homology to immunoglobulin and mucin-like adhesion receptors and to IgA1" see the whole document -----</p>	1-100

Information on patent family members

PC 96/02153

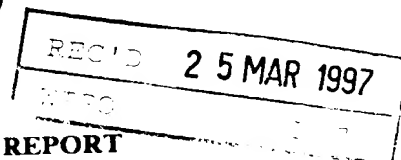
Form PCT/ISA 210 (patent family annex) (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference LKS94-04A2 PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US 96/ 02153	International filing date (day/month/year) 12/02/1996	Priority date (day/month/year) 10/02/1995
International Patent Classification (IPC) or national classification and IPC C12N15/12		
Applicant LEUKOSITE, INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This **REPORT** consists of a total of 4 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consists of a total of _____ sheets.

3. This report contains indications and corresponding pages relating to the following items:

I ☒ Basis of the report

II ☐ Priority

III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

IV ☐ Lack of unity of invention

V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

VI ☐ Certain documents cited

VII ☐ Certain defects in the international application

VIII ☐ Certain observations on the international application

Date of submission of the demand 09/09/1996	Date of completion of this report 25.03.97
Name and mailing address of the IPEA European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Netherlands Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016	Authorized officer M. Cupido Telephone No. (+31-70) 340 3374

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US96/02153

I. Basis of the report

1. This report has been drawn up on the basis of *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*

☒ the international application as originally filed

☐ the description, pages
pages
pages

, as originally filed
, filed with the demand
, filed with the letter of

☐ the claims, Nos.
Nos.
Nos.
Nos.

, as originally filed
, as amended under Article 19
, filed with the demand
, filed with the letter of

☐ the drawings, sheets / fig.
sheets / fig.
sheets / fig.

, as originally filed
, filed with the demand
, filed with the letter of

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.
☐ the drawings, sheets / fig.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2 (c)).

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US96/02153

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos.

51-100

because:

☒ the said international application, or the said claims relate to the following subject matter which does not require an international preliminary examination (specify):

Nos.

claims 51 to 100 are directed to a method of treatment of the human and/or animal body, see Article 34(4)(a)(i) and Rule 67.1(iv).

☐ the description, claims or drawings (indicate particular elements below) or said claims are so unclear that no meaningful opinion could be formed (specify):

Nos.

☐ the claims, or said claims are so inadequately supported by the description no meaningful opinion could be formed.

Nos.

☐ no international search report has been established for said claims

Nos.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US96/02153

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty	Claims	1-50	YES
	Claims		NO
Inventive Step	Claims	1-50	YES
	Claims		NO
Industrial Applicability	Claims	1-50	YES
	Claims		NO

2. Citations and Explanations

I Documents

The following documents have been considered for the purposes of this report:

D1: WO-A-94/13312 (The Board of Trustees of the Leland Stanford University)

D2: The Journal of Immunology 153:517-527 (D.J. Erle et al., 1994)

II Novelty

1. D1 discloses the molecular cloning of a murine Mucosal Addressin Cell Adhesion Molecule (MAdCAM-1). However, the human homolog of MAdCAM-1 has not been identified in the prior art and thus the subject-matter of claims 1-38 and 44-49 is regarded to be novel within the meaning of Article 33(2).

2. Antibodies MECA-89 and MECA-367 specific for murine MAdCAM-1 have been mentioned in D1. It is however unclear if these antibodies are capable to bind a primate MAdCAM. Hence the subject-matter of claims 39-43 and 50 is considered as novel according to Article 33(2).

III Inventive step

1. D2 is the closest prior art with respect to the question whether the subject-matter in claims 1-50 involves an inventive step. In D2 the expression of the MAdCAM-1 receptor, Integrin α 4 β 7 on human leukocytes is studied using murine MAdCAM-1. The problem underlying the present invention in view of D2 is the provision of further ligands which bind Integrin α 4 β 7. The solution provided by the application consists of the human homologue of MAdCAM-1 which may be advantageous over its murine counterpart as a medicament in human medicine. This protein could not be derived in any way from the prior art and thus is the subject-matter of claims 1-50 regarded to involve an inventive step as required by Article 33(3).

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 96/02153

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 51-100
because they relate to subject matter not required to be searched by this Authority, namely:
REMARK: ALTHOUGH CLAIMS 51-100 ARE DIRECTED TO A METHOD OF TREATMENT OF THE HUMAN BODY THE SEARCH HAS BEEN CARRIED OUT AND BASED ON THE ALLEGED EFFECTS OF THE COMPOSITION.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

information on patent family members

Functional Application No

PCT/US 96/02153

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9413312	23-06-94	AU-B- 5675794	04-07-94

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 96/02153

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>NATURE, vol. 363, 3 June 1993, LONDON GB, pages 461-464, XP002006076 M.J.BRISKIN ET AL.: "MAdCAM-1 has homology to immunoglobulin and mucin-like adhesion receptors and to IgA1" see the whole document</p> <p>-----</p>	1-100

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 96/02153

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C07K14/705 C12N15/62 C07K19/00 C07K16/28
G01N33/566

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO,A,94 13312 (THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY) 23 June 1994 see the whole document ---	1-100
A	JOURNAL OF IMMUNOLOGY, vol. 153, no. 1, 1 July 1994, BALTIMORE US, pages 517-527, XP002006075 D.J.ERLE ET AL.: "Expression and function of the MAdCAM-1 receptor, integrin alpha4beta7, on human leukocytes" see page 525, left-hand column --- -/-	1-100

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

19 June 1996

Date of mailing of the international search report

27.06.96

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3016

Authorized officer

Cupido, M

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification⁶ :

C12N 15/12, C07K 14/705, C12N 15/62,
C07K 19/00, 16/28, G01N 33/566

A1

(11) International Publication Number:

WO 96/24673

(43) International Publication Date:

15 August 1996 (15.08.96)

(21) International Application Number: PCT/US96/02153

(22) International Filing Date: 12 February 1996 (12.02.96)

(30) Priority Data:

08/386,857 10 February 1995 (10.02.95) US
08/523,004 1 September 1995 (01.09.95) US

(60) Parent Applications or Grants

(63) Related by Continuation

US 08/386,857 (CIP)
Filed on 10 February 1995 (10.02.95)
US 08/523,004 (CIP)
Filed on 1 September 1995 (01.09.95)

(71) Applicant (for all designated States except US): LEUKOSITE,
INC. [US/US]; 215 First Street, Cambridge, MA 02142
(US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): BRISKIN, Michael, J.
[US/US]; 28 Harbell Street, Lexington, MA 02173 (US).
RINGLER, Douglas, J. [US/US]; 382 Ocean Avenue #1008,
Revere, MA 02151 (US). PICARELLA, Dominic [US/US];

9 Kay Street, Sudbury, MA 01776 (US). NEWMAN, Walter
[US/US]; 3 Durham Street #3, Boston, MA 02115 (US).

(74) Agents: BROOK, David, E. et al.; Hamilton, Brook, Smith &
Reynolds, Two Militia Drive, Lexington, MA 02173 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY,
CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS,
JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD,
MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent
(AZ, BY, KG, KZ, RU, TJ, TM), European patent (AT, BE,
CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT,
SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML,
MR, NE, SN, TD, TG).

Published

With international search report.

Before the expiration of the time limit for amending the
claims and to be republished in the event of the receipt of
amendments.

(54) Title: MUCOSAL VASCULAR ADDRESSINS AND USES THEREOF

(57) Abstract

The present invention relates to isolated and/or recombinant nucleic acids which encode primate MAdCAMs, and to proteins or polypeptides referred to herein as isolated and/or recombinant primate MAdCAMs. The invention further relates to recombinant nucleic acid constructs, comprising a nucleic acid which encodes a primate MAdCAM of the present invention, a portion thereof, or a variant; to host cells comprising such constructs, useful for the production of recombinant proteins; the use of nucleic acids and/or proteins in assays to identify inhibitors (e.g., antagonists) of primate MAdCAM function; and to antibodies reactive with primate MAdCAM, which are useful in *in vitro* methods, diagnostic and/or therapeutic applications. The invention also relates to the treatment of individuals, particularly humans, suffering from a disease (e.g., inflammatory bowel disease) associated with leukocyte recruitment to the gastrointestinal tract or other tissues, for example, as a result of binding of leukocytes to cells expressing the molecule MAdCAM (gut-associated endothelium), comprising administering to the individual an effective amount of an agent, such as an antibody which inhibits the binding of leukocytes to MAdCAM.